IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Ray W. Wood et al.
Title:	METHODS OF ADMINISTERING LIQUID DROPLET AEROSOLS OF NANOPARTICULATE DRUGS
Appl. No.:	09/577,489
Filing Date:	5/25/2000
Examiner:	James Henry Alstrum Acevedo
Art Unit:	1616
Confirmation Number:	7761

DECLARATION UNDER 37 C.F.R. §1.132

The undersigned, H. William Bosch, hereby declares as follows:

I. Background of H. William Bosch

1. I received my Ph.D. degree in 1987 from the University of Pennsylvania in chemistry. I have been working in the field of nanoparticulate drug technology since 1991, when I joined Sterling Winthrop Pharmaceuticals Research Division.

2. The portion of Sterling Winthrop Pharmaceuticals Research Division involved in nanoparticulate drug technology was sold and became known as NanoSystems. This business was then sold and became known as Elan Drug Technologies. Intellectual property developed at Elan Drug Technologies is owned by Elan Pharma International Ltd., which is the assignee of the above-referenced patent application.

3. Currently I am the Director of Pharmaceutical Research at iCeutica, with offices at 1 Crescent Drive, Suite 400, Navy Yard Corporate Center, Philadelphia PA 19112.

II. Nebulization of Beclomthasone Formulations

5. Four beclomethasone diproprionate (BDP) formulations comprising polyvinyl alcohol as a surface stabilizer were tested for nebulization. The nebulizers contained either a volume of about 2 ml or about 6 ml of the formulation to be tested. The formulations are detailed in Table 1.

Table 1

Formulation	Form	Surface Stabilizer Concentration	Test Volume (ml)
Micro I	Suspension comprising raw, micronized beclomethasone diproprionate particles	2.5%	1.85
Nano II	Dispersion comprising nanoparticulate beclomethasone diproprionate particles	2.5%	1.85
Nano III	Dispersion comprising nanoparticulate beclomethasone diproprionate particles	0.1%	1.85
Nano IV	Dispersion comprising nanoparticulate beclomethasone diproprionate particles	0.1%	5.85

6. The nebulization output for each formulation is detailed in Table 2.

Table 2

Formulation	BDP Fraction Remaining in Nebulizer	BDP Fraction Reaching Impactor
Micro I	~89%	~8%
Nano II	~77%	~18%
Nano III	~62%	~17%
Nano IV	~29%	~35%

7. The data in column 2 of Table 2 demonstrate that a higher fraction of microparticulate BDP composition I remained in the nebulizer compared to the nanoparticulate BDP compositions II-IV. Compositions I and II were equivalent in all respects except for the drug particle size distribution. For microparticulate BDP composition I, about 89% of the BDP remained in the nebulizer; whereas in the case of nanoparticulate BDP composition II, about 77% of BDP remained in the nebulizer. Nanoparticulate compositions III and IV also had smaller fractions of BDP remaining in the nebulizer (62% and 29% respectively) compared to the microparticulate formulation I.

8. The data in column 3 of Table 2 demonstrate that a greater fraction of nanoparticulate BDP formulation II reached the impactor as compared to the microparticulate BDP formulation I. Specifically, only about 8% of the microparticulate BDP formulation reached the impactor, while about 17% of the nanoparticulate BDP formulation reached the impactor. Nanoparticulate compositions III and IV also had greater fractions of BDP reaching the impactor (17% and 35% respectively) compared to the microparticulate formulation I.

CONCLUSION

9. The data described herein demonstrate that the nanoparticulate beclomethasone diproprionate formulations (II-IV) achieved more efficient nebulization than the control formulation (I) comprising microparticulate beclomethasone diproprionate.

10. I declare that the statements made herein of my knowledge are true and all statements on information and belief are believed to be true; and further these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing therein.

H. William Bosch

H. William Bosch

August 5, 2010

Date